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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,843	12/22/2000	Shui-on Leung	018733-0996	9659

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/741,843	LEUNG ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 95-100,105-108,110,113,126 and 127 is/are pending in the application. (115,)

4a) Of the above claim(s) 105-108 and 110 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 95-100,113,115,126,127 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Regarding applicants comments, antibodies with substituted FR regions do not read on the elected species because they contain amino acids different from those found in the elected species. The claims reading on CDRs derived from the elected species have been included as part of the elected species. It is noted that the species election of 12/18/03 referred to a specific antibody with a specific amino acid sequence and referred to a choice of said sequence with or without exogenous FR regions (SEQ IDs 2 and 4 versus antibody of claim 111). Murine and human FRs have different amino acid sequences and are functionally distinct (for example with regards to immunogenicity upon human administration).

2. Claims 95-100,113,115,126,127 are under consideration as per reading on the previously elected species (chimeric antibody, aka antibody of SEQ. IDs 2 and 4). Claim 115 is now under consideration because it has been amended to depend from pending claim 113.

3. The amendment filed 12/12/06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. The abstract raises the issue of new matter in the second line (fragments thereof), wherein there is no support for said fragments in the specification as originally filed. The abstract raises the issue of new matter in the recitation of "A humanized LL2 monoclonal antibody further comprises a framework sequence of human light and heavy chains variable regions" because it does not state where the FRs are attached to the CDRs and the specification discloses said FRs only as per found attached to CDRs as is normally found in antibodies.

Applicant is required to cancel the new matter in the reply to this Office Action.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 95-100,113,115,126,127 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25-27 of U.S. Patent No. 6,187,287. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the two sets of claims differ in scope, both sets of claims encompass nucleic acids/expression vectors encoding antibodies or fragments containing SEQ. ID. No 2 and 4 or nucleic acids comprising the CDRs contained in said sequences wherein said antibodies bind the antigen bound by LL2 antibody (CD22). Myeloma cells were known in the art as host cells for vectors encoding antibodies. The nucleic acid sequences can also contain human constant region sequences (see claim 25). It would have been obvious to produce the nucleic acid encoding the fragments of claim 115, wherein the antibody fragment was produced for usage in art known applications wherein such fragments were used (immunoassays, etc).

Regarding applicants comments, both sets of claims encompass the same chimeric antibodies with the same variable region amino acid sequences (aka SEQ. ID. No. 2 and 4 wherein said sequences contain the CDRs recited in the claims), wherein said antibodies would contain art known human constant regions. Therefore, the antibodies would inherently have the properties recited in claims 25-27.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 95-100,113,115,126,127 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Previously present grounds of rejection not restated in this Office Action are withdrawn in view of the amended claims or cancellation of claims that have been cancelled.

There is no support in the specification as originally filed for the nucleic acids of claims 95-100. The claimed inventions constitute nucleic acids encoding chimeric antibody heavy or light chains that contain a single CDR recited in the claims in the absence of the other CDRs found in the parent LL2 antibody. There is no disclosure in the specification as originally filed of such nucleic acids. The various cited Figures to which applicant refers discloses chimeric or humanized nucleic acids encoding antibodies containing heavy and light chains wherein said heavy or light chain contain all of the CDRs found in the parent LL2 antibody. Similarly, the cited passages of the specification disclose methods of making chimeric or humanized antibodies which contain all of the CDRs found in the parent antibody. The claimed inventions encompass antibodies which contain a single CDR derived from the parent LL2 antibody in association with nonLL2 CDRs wherein nucleic acid encoding such antibodies were not disclosed in the specification as originally filed.

The CAFC stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1997) that:

3. Patentability/Validity -- Specification -- Written description .(115.1103) Patent's entitlement to earlier filing date extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed; one shows that one is "in possession" of invention of patent by describing invention, with all its claimed limitations, not that which makes it obvious, and although prior application need not describe claimed subject matter in exactly same terms used in claims, prior specification must contain equivalent description of claimed subject matter, and description which renders obvious invention for which earlier filing date is sought is not sufficient.

The CAFC stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that:

The invention is, for purposes of the 'written description' inquiry, whatever is now claimed .") (emphasis in original). One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Although the exact terms need not be used in haec verba , see Eiselstein v. Frank , 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (" [T]he prior application need not describe the claimed subject matter in exactly the same terms as used in the claims.. . ."), the specification must contain an equivalent description of the claimed subject matter. *A description which renders obvious the invention for which an earlier filing date is sought is not sufficient.*

There is no support in the specification as originally filed for the nucleic acid(or vectors or cells containing said nucleic acids) of claims 113,126,127. The specification discloses chimeric LL2 antibody wherein said nucleic acids encode all of the CDRs and FRs derived the murine LL2 antibody. The claims encompass nucleic acids encoding chimeric antibodies wherein the heavy and or light chain variable regions contain FR regions not derived from LL2 and there is no disclosure of such nucleic acids in the specification as originally filed. For example, there is no disclosure in the specification of chimeric antibodies with FRs derived from other murine species. Regarding

applicants comments, claim 113 encompasses FRs derived from other than the parent murine LL2 antibody. The claims encompass nucleic acids encoding chimeric antibodies wherein the heavy and or light chain variable regions contain FR regions not derived from LL2 and there is no disclosure of such nucleic acids in the specification as originally filed. For example, there is no disclosure in the specification of chimeric antibodies with FRs derived from other murine species.

There is no support in the specification as originally filed for the expression vectors of claims 126,136,146. The specification discloses use of "mammalian expression vectors", but not the use of vectors per se wherein said term would encompass nonmammalian expression vectors. Regarding applicants comments, Figure 3 (see brief description of drawings) and Example 3 are limited to the disclosure of "mammalian expression vectors".

There is no support in the specification as originally filed for the fragments of claim 115. Nucleic acids encoding chimeric antibody fragments of claim 115 are not disclosed in the specification as originally filed.

There is no written description of the claimed inventions in the specification as originally filed (the claimed inventions constitute new matter).

8. Regarding claims 95-100,113,115,126,127 and the application of prior art, for the same reasons that said claims constitute new matter, they are not entitled to priority to the parent applications to which priority is claimed.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 95-100,113,126,127 stand rejected under 35 U.S.C. 102(b) as being anticipated by Leung et al. (US Patent 5,789,554). Applicants arguments have been considered and deemed not persuasive.

Leung et al. teach nucleic acids encoding the chimeric LL2 antibody which contains the nucleic acids encoding the variable heavy and light chains of the murine LL2 wherein said chains have the CDRs recited in the claims (see Example 4 and Figures 4a and 4b). Leung et al. teach vectors and a myeloma host cell containing said nucleic acids (see Example 4). All of the instant polynucleotide claims are considered "open" and therefore encompass the nucleic acids encoding the chimeric LL2 antibody. Leung et al. disclose that the nucleic acids can also include human constant regions (see Example 4). Regarding applicants comments, whilst Leung et al. discloses embodiments that anticipate the claimed inventions, the scope of the claims under consideration also encompass additional embodiments which constitute new matter as per above.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 95-100,113,115,126,127 are rejected under 35 U.S.C. § 103 as being unpatentable over Goldenberg et al. (J. Clin. Oncol.) in view of Morrison et al., Cabilly et al., Boss et al., Orlandi et al., and Huston et al. (US Patent 5,258,498). Applicants arguments have been considered and deemed not persuasive.

Goldenberg et al. teach the murine LL2 monoclonal antibody and hybridoma producing said antibody (see page 549). Goldenberg et al. teach that administration of said antibody provokes a HAMA response in some patients (see abstract). The claimed nucleic acids encode peptides which encompass or contain the CDR(s) found in the VH and VL of said antibody. The hybridoma which produces murine LL2 antibody produces the claimed nucleic acids which encode the VH and VL of said antibody. Goldenberg et al. do not teach the claimed isolated nucleic acids and vectors or host cells containing said nucleic acids. Morrison et al. teach chimeric antibodies containing variable regions from a known mouse antibody attached to human constant regions (see abstract and columns 1-8). Morrison et al. disclose nucleic acids encoding variable light and heavy chains of a murine antibody attached to nucleic acids encoding human constant regions (see column 3-6). Morrison et al. disclose that the nucleic acids encoding the murine variable regions would be obtained by routine experimentation (see column 3). The nucleic acids are expressed in vectors (see column 6, penultimate paragraph) which can be transfected into myeloma cells (see column 7, second paragraph). Orlandi et al. also teaches primers and the use of said primers to clone DNA encoding murine variable heavy and light regions (eg. see abstract and page 3833, second column and page 3834). Both Cabilly et al. and Boss et al. disclose methods for the determination of nucleic acids encoding VH and VL of any known antibody. Huston et al. teaches that regarding the determination of the sequence of VH and VL from any desired antibody that "Such sequence analysis is now conducted routinely." (see column 13).

Thus, the art taught the murine LL2 antibody, nucleic acids encoding VH and VL and methods of producing VH and VL amino acid sequences encoding any known antibody wherein said methods used a hybridoma which produced said antibody. Said nucleic acids would have been used to produce chimeric antibodies as per taught by Morrison et al. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Goldenberg et al. teach the murine LL2 monoclonal antibody wherein said antibody is produced by a hybridoma, and the references cited in this rejection teach chimeric antibodies, nucleic acids encoding VH and VL, and methods of making chimeric

antibodies based on the nucleic acid sequence of any known antibody VH and VL, and methods of determining the nucleic acid sequence of any known antibody VH and VL. Cabilly et al. disclose that the chimeric antibodies can be produced as Fab (see column 5, first complete paragraph). All variable regions are structurally similar in that they contain similar numbers of amino acids organized in a similar fashion (eg. they contain a VH and VL wherein the VH and VL contain framework and variable region amino acids). Regarding motivation to create the claimed invention, Goldenberg et al. disclose clinical use of the murine LL2 antibody and the art recognized the advantages of antibodies encoded by nucleic acids encoding chimeric antibodies (see Morrison et al., column 7, last paragraph, continued on column 8, Orlandi et al., page 3833, first column, first paragraph).

Regarding applicants comments, there is no evidence of record regarding the lack of public availability of the LL2 antibody or hybridoma producing said antibody. Regarding the Goldenberg and Hansen declarations, said declarations refer to vectors encoding humanized LL2 which are not germane to the instant rejection. Said declarations do not address the public availability of the LL2 antibody or hybridoma.
Regarding applicants comments in page 11 of the instant amendment, the MPEP section 716.01(c), states:
ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE The arguments of counsel cannot take the place of evidence in the record. In re *Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).*

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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